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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,158	05/14/2001	Lars Eyde Theill	A-686A	8931

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AMGEN INCORPORATED
MAIL STOP 27-4-A
ONE AMGEN CENTER DRIVE
THOUSAND OAKS, CA 91320-1799

EXAMINER
CANELLA, KAREN A

ART UNIT	PAPER NUMBER
1642	

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/855,158	Applicant(s) Theill et al
	Examiner Karen Canella	Art Unit 1642

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-17* _____ is/are pending in the application.

4a) Of the above, claim(s) *1-12* _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *13-17* _____ is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *7, 8*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election with traverse of Group II drawn to compositions of matter comprising SEQ ID NO:7, 13 and 16. The traversal is on the ground that the restriction is improper as it separates the methods of treatment comprising Group II from the compositions of Group II and that any search done for the compositions of Group II would result in identifying references for Group I. This has been considered but not found persuasive. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the composition of Invention II can be used in a process to raise an antibody. As to the question of burden of search, the claims of Groups I and II are classified differently, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group.

However, the policies set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86 will be followed. Method claims limited to the scope of the allowable product claims will be rejoined and examined at the time the product claims are indicated as being allowable.

For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

2. Claims 1-17 are pending. Claims 1-12, drawn to non-elected inventions, are withdrawn from consideration. Claims 13-17 are examined on the merits.

Claim Objections

3. Claim 16 and 17 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 16 is drawn to a composition comprising a specific-binding partner for TACI and BCMA as P1 and P2. Claim 14 is drawn to a composition comprising a region of TACI and BCMA as P1 and P2, as P1 and P2. Claim 14 cannot comprising a specific binding partner for TACI or BCMA, as it is drawn to TACI and BCMA, not specific binding partners thereof, therefore claim 16 cannot depend on claim 14.

Claim Rejections - 35 USC § 112

4.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites a composition wherein F1 is a vehicle. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "vehicle" in claim 13 is defined by the specification to a molecule which prevents degradation and/or increases half life, reduces toxicity, reduces immunogenicity, or increases biological activity of a therapeutic protein, and a preferred embodiment of a vehicle is taught by the specification to be the Fc region of an immunoglobulin. However, the ordinary meaning of a vehicle is "a substance without therapeutic action, an excipient." which would exclude the Fc region of an antibody and a protein which has therapeutic action, such as one which would increase the biological activity of a protein. Amendment of the claim to delete the definition of F1 as that of a vehicle and incorporate specifically defined substances, such as those discussed on page 13, line 20 to page 14 line 2 would obviate this rejection.

Claims 13, 15 and 16 set forth molecular structures without defining the meaning of the "L".

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Tschopp (WO 99/12965, reference B15 of the IDS filed September 17, 2001). Claim 16 is drawn to a composition comprising a molecular determinant comprising a vehicle followed by an L region followed by P1 followed by an L region followed by P2. For the reasons set forth in the rejection under 112, second paragraph above, and the claim objection above, the metes and bound of the claim is unclear with respect to the dependency on claim 14 and the structural requirements of the "L". However, it is reasonable to presume that P1 and P2 are independent of each other, and that the c and d indices for L can be equal to zero, as this is the case for claim 13. As P1 and P2 are independent of each other they can also be identical to each other in the case where the aforesaid c and d indices are equal to zero. Thus the claim can be read as encompassing the extracellular domain of APRIL fused to a marker or tagging sequence. Tschopp discloses the fusion of the 5' extracellular domain which constitutes the receptor binding site of APRIL to a marker or tagging sequence (page 32, lines 13-25). The chimeric fusion protein would inherently bind TACI and BCMA, thus fulfilling the specific requirement that P1 and P2 be specific binding partners for TACI and BCNA.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross et al (Nature, April 2000, Vol. 404, pp. 995-999, reference C22 of the IDS filed September 17, 2001) in view of Tschopp (WO 99/12965, reference B15 of the IDS filed September 17, 2001) and Naismith et al (Structure, 1996, Vol. 4, pp. 1251-1262). Claim 13 is drawn to a composition comprising a molecular determinant comprising SEQ ID NO:16, SEQ ID NO:7 and/or SEQ ID NO:13. The specification teaches that these are the cysteine rich regions in the extracellular domain of TACI, BCMA and the consensus sequence for TACI/BCMA. The specification and

the claims specify that the full length extracellular region is excluded from this molecular determinant. Claim 13 attaches these amino acid sequences together by means of an "L" group having an indices in the range of 0 to 1. Claim 13 also specifies that the linked amino acid sequences can be further attached to a vehicle. The specification defines an exemplary vehicle as consisting of the Fc region of an immunoglobulin domain (page 13, lines 2-23).

Gross et al teach the compositions comprising the extracellular domains of TACI and BCMA fused to the Fc portion of a human immunoglobulin (page 997, second column, lines 11-13). Gross et al teach that these chimeric proteins inhibited ZTNF4, a tumor necrosis factor ligand implicated in autoimmune disease (bridging paragraph of pages 997-998). Gross et al suggest that TACI-IgG is promising in the treatment of autoimmune disease in humans. Thus Gross et al teach compositions comprising the complete extracelluar domains of TACI and BCMA. Gross et al do not teach a fusion protein comprising only the consensus sequences of TACI and BCMA.

Naismith et al teach motifs that identify the cystine rich extracellular domains within tumor necrosis factor receptors (page 1255-1256, first paragraph under the heading "Modular Structure of sTNF-R).

Tschopp teaches that the cysteine rich extracellular domains of the TNF receptor family is a ligand binding region.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to construct a chimeric protein comprising single or multiple amino

acid sequence of the consensus regions of TACI and BCMA fused to the Fc regions of an immunoglobulin. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Tschopp regarding the cysteine rich ligand binding regions of the extracellular domains of TNF receptors, and the teachings of Gross et al regarding the suppression of B-cell autoimmune disease in mice and the similarity of said autoimmune disease with systemic lupus erythematosus. One of skill in the art would be motivated to attach multiple consensus regions together in order to better trap the ligand zTNF4, the overexpression of which gives symptoms consistent with systemic lupus erythematosus.

10. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tschopp (WO 99/12965, reference B15 of the IDS filed September 17, 2001) in view of Ward (WO 97/34631, reference B15 of the IDS filed Septmeber 17, 2001). Claim 17 is drawn to the composition of claim 16 wherein the vehicle is an Fc receptor.

Tschopp teaches the composition of claim 16 wherein the vehicle is a marker or tagging sequence. Tschopp teaches that such a chimeric protein can be used to isolate a receptor binding to APRIL ligand. Tschopp does not teach fusion of the extracellular potion of APRIL to the Fc domain of an immunoglobulin region.

Ward teaches that recombinant fusion of proteins or proteins domains of interest with the Fc region of an immunoglobulin will generate chimeric proteins with increased stability and longevity for therapeutic and diagnostic uses.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to fuse the extracellular domain of APRIL to the Fc region of an immunoglobulin. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Ward on the greater stability and half-life in vivo of the Fc fusion proteins and the teachings of Tschopp on the use of the extracellular domain of APRIL in the identification of a receptor which binds to APRIL.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentable distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F. 3d 1428, 46 USPQ2d 1226 (Fed Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

13. Claims 16 and 17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27-30 of copending Application No. 09/854,864. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 27-30 of the '864 application, as drawn to specific binding partners of TACI and BCMA can atticipate claim 16. Claim 31 of the '864 application, as drawn to specific binding partners of TACI and BCMA, anticipates claim 17..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

January 13, 2003